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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,626	09/26/2003	Amy F.T. Arnsten	MPI-0003	8080

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/672,626	ARNSTEN ET AL.	
	Examiner	Art Unit	
	Renee Claytor	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 18-21* is/are pending in the application.

4a) Of the above claim(s) *5-9,11 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 10, 12, 14, 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 11/6/2007 is acknowledged. Currently, claims 1-14 and 18-21 are pending, and claims 1-4, 10, 12, 14, and 18-21 are under examination.

In light of Applicants amendment to claims 18-20, the claim objection is hereby withdrawn.

Applicants argue the 35 USC 112, first paragraph rejection that the claims as amended are enabled. In particular, Applicants argue that one of ordinary skill in the art would understand that a CNS disorder associated with impaired prefrontal cortical function associated with activation of protein kinase C is those specific diseases among a list on page 8 of the Remarks (first paragraph). Further Applicant's have amended Claim 1 to only include the compound of Formula I, and assert that Claim 1 is now enabled for all disclosed compounds.

In response to the above arguments, it is apparent to the Examiner that the Applicants have amended claim 1 to narrow the list of CNS disorders that are thought to be treated in the invention. However, the list that is put forth on page 8 of the remarks include disorders such as bipolar disorder, attention deficit hyperactivity disorder and Alzheimer's disease (behavioral symptoms) just to name a few. All of these disorders have different etiologies and symptamologies leading to a different characterization of each compound. Because a pharmaceutical composition may treat bipolar disorder, does not necessarily mean that it will treat disorders such as attention deficit hyperactivity disorder or behavioral symptoms associated with Alzheimer's disease. It is considered that the claim limitation of treating a CNS disorder associated with

impaired prefrontal cortical function associated with protein kinase C is a broad limitation of which the specification is not fully enabled for.

Further, the specification outlines specific examples of treating bipolar disorder with chelerythrine; however, there are no other examples of any other compound of formula (I). Each side group of Formula (I) may lead to different pharmacological actions, bioavailability and solubilities and it is considered that the specification is not enabled for Formula (I) with all of the substituents listed. Therefore, the 35 USC 112 rejection is maintained.

Applicants have amended claim 20 to remove the claim limitation of prevention. Accordingly, the rejection is withdrawn.

Applicant's arguments over the 35 USC 103(a) rejection have been fully considered. In particular, Applicants argue that one of ordinary skill in the art would not have expected that systemically-administered chelerythrine would interact with protein kinase C in the brain because it was not expected that chelerythrine would cross the blood brain barrier and have no reasonable expectation of success that chelerythrine could be used to treat bipolar disorder. Applicants discuss that chelerythrine has been used *in vivo* to treat peripheral disorders and also has been used in local injection in nervous system disorders. Applicant's arguments are found persuasive and the 35 USC 103(a) rejection is hereby withdrawn.

Claim Rejections – 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, there is no indication in the specification that "n is from 0 to 3". The specification on page 5 teaches that "n is 0 to 3".

Claims 1-3, 10, 12, 14 and 18-21 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating certain types of CNS disorder associated with impaired prefrontal cortical function associated with activation of protein kinase C or a working memory deficit, including bipolar disorder with chelerythrine, does not reasonably provide enablement for all CNS disorders associated with activation of protein kinase C with all compounds of formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set

forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The Nature of the Invention: The rejected claims 1-3, 10, 12, 14 and 18-21 are drawn to a method for treating a CNS disorder associated with activation of protein kinase C or a working memory deficit in a subject comprising administration an effective amount of a compound of formula (I).

(2) The state of the prior art: The state of the art regarding treatment of various types of CNS disorders and impaired cognitive performance is high. However the state of the art regarding treatment for all CNS disorders associated with activation of protein kinase C with all compounds according to formula (I) is underdeveloped. The skilled artisan would view that the treatment of all types of CNS disorders and impaired cognitive performance with all compounds of formula (I) is highly unlikely.

(3) The relative skill of those in the art: The relative skill of those in the art is high.

(4) The breadth of the claims: Claims 1-3, 10, 12, 14 and 18-21 embrace a method for treating a CNS disorder or impaired cognitive performance in a subject comprising administration of an effective amount of a compound of formula (I).

(5) The amount of guidance or direction presented: In the instant case, working examples are presented for treating manic episodes and learning and memory tasks with chelerythrine in the specification on pages 19-23, in which chelerythrine was shown to increase performance on learning and memory tasks as well as improve the stress response (involving manic episodes). However, there are a lack of working examples presented in the specification as filed showing how to treat all CNS disorders associated with activation of protein kinase C with all compounds of formula (I). For example, the compounds of formula (I) have many possible substitutions that can be applied to R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, and R^{10} thereby leading to distinct chemical compounds. Because each compound is distinct structurally, each compound may have different reactivity, solubility, oral bioavailability etc. Note that lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP § 2164.

(6) The presence or absence of working examples: Applicant provides working examples for treating learning and memory disorders and bipolar disorders with chelerythrine. However, Applicant does not provide any working examples for treating all CNS disorders associated with activation of protein kinase C with all compounds for formula (I).

(7) The quantitation of experimentation necessary: Claims 1-3, 10, 12, 14 and 18-21 read on a method for treating a CNS disorder associated with activation of protein kinase C or a working memory deficit comprising administration of a compound of formula (I). As discussed above, the specification provides examples for treating

learning and memory disorders and bipolar disorders with chelerythrine but the specification fails to provide support for treating all CNS disorders associated with activation of protein kinase C. As discussed above, compounds of formula (I) have distinct structures, lending to different reactivity, solubility and oral bioavailability etc. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is 571-272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor